



Amendment

In the Claims:

1. (Currently amended): A vector for delivery of a virus to a target cell within a host animal, ~~consisting essentially of~~ comprising a cell-targeting ligand non-covalently bound directly to said virus, wherein said ligand binds directly to a receptor on said target cell.

2. (Original): The vector of claim 1 wherein said virus and said ligand are not naturally associated with each other.

3. (Original): The vector of claim 1, wherein said virus is comprised of a therapeutic nucleic acid.

4. (Original): The vector of claim 1, wherein said virus is comprised of a nucleic acid that encodes a therapeutic peptide or protein.

5. (Original): The vector of claim 1, wherein said virus is comprised of a nucleic acid that encodes wild-type p53.

6. (Original): The vector of claim 1, wherein said virus is a retrovirus or an adenovirus.

7. (Original): The vector of claim 1, wherein said virus is selected from the group consisting of adeno-associated virus, herpes simplex virus, cytomegalovirus, vaccinia virus, fowlpox virus, canarypox virus and Sindbis virus.

8. (Original): The vector of claim 1, wherein said virus is a chimeric virus, a hybrid virus, or a recombinant virus.

9. (Original): The vector of claim 1, wherein said cell-targeting ligand is selected from the group consisting of proteins, peptides, hormones, antibodies and antibody fragments.

10. (Original): The vector of claim 1, wherein said cell-targeting ligand is a native protein or a recombinant protein.

11. (Original): The vector of claim 1, wherein said cell-targeting ligand is selected from the group consisting of insulin, toxins, EGF, VEGF, FGF, IGF, heregulin, a viral protein, a bacterial protein, estrogen and progesterone.

12. (Original): The vector of claim 1, wherein said cell-targeting ligand is transferrin.

13. (Original): The vector of claim 1, wherein said cell-targeting ligand and said virus are present at a ratio in the range of 100 to 1,000,000 ligand molecules per virion.

14. (Original): The vector of claim 1, wherein said cell-targeting ligand and said virus are present at a ratio in the range of 6,700 to 400,000 ligand molecules per virion.

15. (Currently amended): The vector of claim 1, wherein said cell-targeting ligand and said virus are present at a ratio in the range of 1 μ g to 10 mg of said ligand per 10^{10} ~~virion~~ virions.

16. (Currently amended): The vector of claim 1, wherein said cell-targeting ligand and said virus are present at a ratio in the range of 10 μ g to 600 μ g of said ligand per 10^{10} ~~virion~~ virions.

17. (Currently amended): A method for preparing a vector for the systemic delivery of a virus to a target cell, said vector ~~consisting essentially of~~ comprising a cell-targeting ligand non-covalently bound directly to said virus, comprising mixing said cell-targeting ligand with said virus in an aqueous medium, whereby said ligand non-covalently binds directly to said virus.

18. (Original): The method of claim 17, wherein said aqueous solution includes one or more of a buffering agent, an osmolarity adjusting agent, or an antibiotic.

19. (Currently amended): A method for targeting delivery of a nucleic acid to cancer cells of an animal suffering from head and neck cancer, bladder cancer, breast cancer, thyroid cancer, ovarian cancer, prostate cancer, melanoma or lymphoma, comprising administering systemically to said animal a viral vector ~~consisting essentially of~~ comprising a virus comprising said nucleic acid and a cell-targeting ligand which is non-covalently bound directly to said virus and binds directly to a receptor which is over-expressed on said cells.

20. (Original): The method of claim 19, wherein said animal is human.

21. (Canceled).

22. (Original): The method of claim 19 wherein said therapeutic agent is administered parenterally.

23. (Original): The method of claim 19 wherein said therapeutic agent is administered intravenously or intra-arterially.

24. (Canceled).

25. (Previously presented): The method of claim 19, 39, 40 or 41 wherein said vector encodes wild-type p53.

26. (Previously presented): The method of claim 19, 39, 40 or 41 wherein said cell-targeting ligand is transferrin.

27. (Original): The method of claim 19 wherein said therapeutic agent is administered to an animal receiving chemotherapy in addition to said therapeutic agent.

28. (Original): The method of claim 19 wherein said therapeutic agent is administered to an animal receiving radiation treatment in addition to said therapeutic agent.

29. (Previously presented): The method of claim 19, 39, 40 or 41 wherein said virus is comprised of a nucleic acid encoding wild-type p53 and said cell-targeting ligand is transferrin.

30-31. (Canceled).

32. (Original): The vector of claim 1, wherein said virus is an adenovirus comprising a therapeutic nucleic acid and said ligand is transferrin or EGF.

33. (Original): The vector of claim 1, wherein said virus is an adenovirus and said ligand as an antibody fragment.

34. (Original): The vector of claim 32, wherein said adenovirus comprises a nucleic acid that encodes wild-type p53.

35. (Original): The vector of claim 33, wherein said adenovirus comprises a nucleic acid that encodes wild-type p53.

36. (Original): The vector of claim 1, wherein said virus is a retrovirus or herpes simplex virus comprising a therapeutic nucleic acid and said ligand is transferrin.

37. (Original): The method of claim 19, wherein said virus is an adenovirus, a retrovirus or a herpes simplex virus.

38. (Previously presented): The method of claim 37, wherein said virus is an adenovirus.

39. (Currently amended): A method of specifically targeting and sensitizing cancer cells to radiation or chemotherapy which comprises systemically administering to a person suffering from cancer a viral vector complex ~~consisting essentially of~~ comprising an admixture of (1) a virus comprising a nucleic acid which will sensitize

said target cells to radiation or chemotherapy and (2) a targeting ligand which is bound directly and non-covalently to said virus and will bind directly to said cancer cells such that said nucleic acid is delivered to said cancer cells; wherein said cancer cells are selected from head and neck cancer, bladder cancer, breast cancer, thyroid cancer, ovarian cancer, prostate cancer, melanoma ~~[[or]]~~ and lymphoma cells, and said cancer cells overexpress a receptor for said ligand.

40. (Currently amended): A method of increasing the levels of expression of a nucleic acid of interest in target cancer cells, which comprises systemically administering an effective amount of a viral vector complex which comprises ~~consists essentially of~~ a virus comprising said nucleic acid and a ligand which is bound directly and non-covalently to said virus and binds directly to a receptor overexpressed on said target cancer cells; wherein expression of said nucleic acid of interest in said target cells sensitizes said cells to radiation or chemotherapy; and further wherein said target cancer cells are selected from the group consisting of head and neck cancer, bladder cancer, breast cancer, thyroid cancer, ovarian cancer, prostate cancer, melanoma and lymphoma cells.

41. (Currently amended): In a method of administering a chemotherapeutic or radiation therapy agent to an animal suffering from head and neck cancer, bladder cancer, breast cancer, thyroid cancer, ovarian cancer, prostate cancer, melanoma and lymphoma, the improvement which comprises:

systemically administering to said animal prior to said chemotherapy or radiation a viral vector complex which comprises ~~consists essentially of~~ (1) a virus comprising a nucleic acid which when expressed in cancer cells sensitizes said cells to radiation or chemotherapy and (2) a ligand which is bound directly to a receptor on said virus and ~~bind~~ binds directly to a receptor on said cancer cells.

42. (Currently amended): A method of specifically targeting and sensitizing cancer cells to radiation or chemotherapy which comprises administering intratumorally to a person suffering from cancer a viral vector complex comprising ~~consisting essentially of~~ an admixture of (1) a virus comprising a nucleic acid which will sensitize said target cells to radiation or chemotherapy and (2) a targeting ligand which is bound directly and non-covalently to said virus and will bind directly to said cancer cells such that said nucleic acid is delivered to said cancer cells; wherein said cancer cells are selected from head and neck cancer, bladder cancer, breast cancer, thyroid cancer, ovarian cancer, prostate cancer, melanoma ~~[[or]]~~ and lymphoma cells, and said cancer cells overexpress a receptor for said ligand.

43 (Currently amended): A method of increasing the levels of expression of a nucleic acid of interest in target cancer cells, which comprises administering intratumorally an effective amount of a viral vector complex which comprises ~~consists essentially of~~ a virus comprising said nucleic acid and a ligand which is bound directly and non-covalently to said virus and binds directly to a receptor overexpressed on said target cancer cells; wherein expression of said nucleic acid of

interest in said target cells sensitizes said cells to radiation or chemotherapy; and further wherein said target cancer cells are selected from the group consisting of head and neck cancer, bladder cancer, breast cancer, thyroid cancer, ovarian cancer, prostate cancer, melanoma and lymphoma cells.

44. (Currently amended): In a method of administering a chemotherapeutic or radiation therapy agent to an animal suffering from head and neck cancer, bladder cancer, breast cancer, thyroid cancer, ovarian cancer, prostate cancer, melanoma and lymphoma, the improvement which comprises:

administering intratumorally to said animal prior to said chemotherapy or radiation a viral vector complex which comprises ~~consists essentially of~~ (1) a virus comprising a nucleic acid which when expressed in cancer cells sensitizes said cells to radiation or chemotherapy and (2) a ligand which is bound directly to a receptor on said virus and ~~bind~~ binds directly to a receptor on said cancer cells.

45. (New): A vector prepared by the method of claim 17.

46. (New): A vector for systemic delivery of a virus to a target cell prepared by mixing a cell-targeting ligand with a virus in an aqueous medium, whereby said ligand non-covalently binds directly to said virus.

47. (New): The vector of claim 46 wherein said virus and said ligand are not naturally associated with each other.

48. (New): The vector of claim 46, wherein said virus is comprised of a therapeutic nucleic acid.

49. (New): The vector of claim 46, wherein said virus is comprised of a nucleic acid that encodes a therapeutic peptide or protein.

50. (New): The vector of claim 46, wherein said virus is comprised of a nucleic acid that encodes wild-type p53.

51. (New): The vector of claim 46, wherein said virus is a retrovirus or an adenovirus.

52. (New): The vector of claim 46, wherein said virus is selected from the group consisting of adeno-associated virus, herpes simplex virus, cytomegalovirus, vaccinia virus, fowlpox virus, canarypox virus and Sindbis virus.

53. (New): The vector of claim 46, wherein said virus is a chimeric virus, a hybrid virus, or a recombinant virus.

54. (New): The vector of claim 46, wherein said cell-targeting ligand is selected from the group consisting of proteins, peptides, hormones, antibodies and antibody fragments.

55. (New): The vector of claim 46, wherein said cell-targeting ligand is a native protein or a recombinant protein.

56. (New): The vector of claim 46, wherein said cell-targeting ligand is selected from the group consisting of insulin, toxins, EGF, VEGF, FGF, IGF, heregulin, a viral protein, a bacterial protein, estrogen and progesterone.

57. (New): The vector of claim 46, wherein said cell-targeting ligand is transferrin.

58. (New): The vector of claim 46, wherein said cell-targeting ligand and said virus are present at a ratio in the range of 100 to 1,000,000 ligand molecules per virion.

59. (New): The vector of claim 46, wherein said cell-targeting ligand and said virus are present at a ratio in the range of 6,700 to 400,000 ligand molecules per virion.

60. (New): The vector of claim 46, wherein said cell-targeting ligand and said virus are present at a ratio in the range of 1 μ g to 10 mg of said ligand per 10^{10} virions.

61. (New): The vector of claim 46, wherein said cell-targeting ligand and said virus are present at a ratio in the range of 10 μ g to 600 μ g of said ligand per 10^{10} virions.